



EVC gene

EvC ciliary complex subunit 1

Normal Function

The *EVC* gene provides instructions for making a protein whose function is unclear. However, it appears to be important for normal growth and development, particularly the development of bones and teeth. The EVC protein is found in primary cilia, which are microscopic, finger-like projections that stick out from the surface of cells and are involved in signaling pathways that transmit information between cells. In particular, the EVC protein is thought to help regulate a signaling pathway known as Sonic Hedgehog, which plays roles in cell growth, cell specialization, and the normal shaping (patterning) of many parts of the body.

EVC and another gene, *EVC2*, are located very close together on chromosome 4. Researchers believe that the two genes may have related functions and that their activity may be coordinated.

Health Conditions Related to Genetic Changes

Ellis-van Creveld syndrome

More than 25 mutations in the *EVC* gene have been reported to cause Ellis-van Creveld syndrome, an inherited disorder characterized by dwarfism, abnormal nails and teeth, and heart defects. The mutations that cause this condition occur in both copies of the *EVC* gene in each cell. These genetic changes disrupt the normal function of the EVC protein or lead to the production of an abnormally small, nonfunctional version of the protein. Although it is unclear how the loss of this protein's function underlies the signs and symptoms of Ellis-van Creveld syndrome, researchers believe that it may prevent normal Sonic Hedgehog signaling in the developing embryo. Problems with this signaling pathway may ultimately lead to the abnormal bone growth and heart defects seen with this condition.

Weyers acrofacial dysostosis

At least one mutation in the *EVC* gene has been found to cause the characteristic features of Weyers acrofacial dysostosis, affecting the development of the teeth, nails, and bones. The signs and symptoms of Weyers acrofacial dysostosis are similar to, but typically milder than, those of Ellis-van Creveld syndrome.

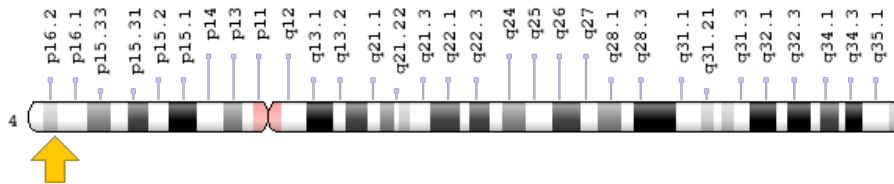
The *EVC* gene mutation that causes Weyers acrofacial dysostosis occurs in one copy of the gene in each cell. It changes a single protein building block (amino acid) in the EVC protein, replacing the amino acid serine with the amino acid proline at position

307 (written as Ser307Pro). It is unclear how this genetic change leads to the specific features of Weyers acrofacial dysostosis. Studies suggest that the abnormal protein interferes with Sonic Hedgehog signaling in the developing embryo, disrupting the normal formation and growth of the teeth, nails, and bones.

Chromosomal Location

Cytogenetic Location: 4p16.2, which is the short (p) arm of chromosome 4 at position 16.2

Molecular Location: base pairs 5,711,197 to 5,829,043 on chromosome 4 (Homo sapiens Annotation Release 108, GRCh38.p7) (NCBI)



Credit: Genome Decoration Page/NCBI

Other Names for This Gene

- DWF-1
- Ellis van Creveld protein
- Ellis van Creveld syndrome
- Ellis van Creveld syndrome protein
- EVC1
- EVC_HUMAN
- EVCL

Additional Information & Resources

Educational Resources

- Developmental Biology (sixth edition, 2000): The Hedgehog Pathway
<https://www.ncbi.nlm.nih.gov/books/NBK10043/#A1063>

Scientific Articles on PubMed

- PubMed
<https://www.ncbi.nlm.nih.gov/pubmed?term=%28EVC%5BTIAB%5D%29+OR+%28EVCL%5BTIAB%5D%29+AND+%28%28Genes%5BMH%5D%29+OR+%28Genetic+Phenomena%5BMH%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3240+days%22%5Bdp%5D>

OMIM

- EVC GENE
<http://omim.org/entry/604831>

Research Resources

- ClinVar
<https://www.ncbi.nlm.nih.gov/clinvar?term=EVC%5Bgene%5D>
- HGNC Gene Symbol Report
http://www.genenames.org/cgi-bin/gene_symbol_report?q=data/hgnc_data.php&hgnc_id=3497
- NCBI Gene
<https://www.ncbi.nlm.nih.gov/gene/2121>
- UniProt
<http://www.uniprot.org/uniprot/P57679>

Sources for This Summary

- Blair HJ, Tompson S, Liu YN, Campbell J, MacArthur K, Ponting CP, Ruiz-Perez VL, Goodship JA. Evc2 is a positive modulator of Hedgehog signalling that interacts with Evc at the cilia membrane and is also found in the nucleus. BMC Biol. 2011 Feb 28;9:14. doi: 10.1186/1741-7007-9-14.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/21356043>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3052239/>
- Howard TD, Guttmacher AE, McKinnon W, Sharma M, McKusick VA, Jabs EW. Autosomal dominant postaxial polydactyly, nail dystrophy, and dental abnormalities map to chromosome 4p16, in the region containing the Ellis-van Creveld syndrome locus. Am J Hum Genet. 1997 Dec;61(6): 1405-12.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/9399901>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1716089/>
- Morrell CH, Brant LJ. Modelling hearing thresholds in the elderly. Stat Med. 1991 Sep;10(9): 1453-64.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/1925173>
- Ruiz-Perez VL, Blair HJ, Rodriguez-Andres ME, Blanco MJ, Wilson A, Liu YN, Miles C, Peters H, Goodship JA. Evc is a positive mediator of Ihh-regulated bone growth that localises at the base of chondrocyte cilia. Development. 2007 Aug;134(16):2903-12.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17660199>

- Ruiz-Perez VL, Goodship JA. Ellis-van Creveld syndrome and Weyers acrodermal dysostosis are caused by cilia-mediated diminished response to hedgehog ligands. *Am J Med Genet C Semin Med Genet*. 2009 Nov 15;151C(4):341-51. doi: 10.1002/ajmg.c.30226. Review.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19876929>
- Ruiz-Perez VL, Ide SE, Strom TM, Lorenz B, Wilson D, Woods K, King L, Francomano C, Freisinger P, Spranger S, Marino B, Dallapiccola B, Wright M, Meitinger T, Polymeropoulos MH, Goodship J. Mutations in a new gene in Ellis-van Creveld syndrome and Weyers acrodermal dysostosis. *Nat Genet*. 2000 Mar;24(3):283-6. Erratum in: *Nat Genet* 2000 May;25(1):125.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/10700184>
- Ruiz-Perez VL, Thompson SW, Blair HJ, Espinoza-Valdez C, Lapunzina P, Silva EO, Hamel B, Gibbs JL, Young ID, Wright MJ, Goodship JA. Mutations in two nonhomologous genes in a head-to-head configuration cause Ellis-van Creveld syndrome. *Am J Hum Genet*. 2003 Mar;72(3):728-32. Epub 2003 Feb 4.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/12571802>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1180248/>
- Sund KL, Roelker S, Ramachandran V, Durbin L, Benson DW. Analysis of Ellis van Creveld syndrome gene products: implications for cardiovascular development and disease. *Hum Mol Genet*. 2009 May 15;18(10):1813-24. doi: 10.1093/hmg/ddp098. Epub 2009 Feb 27.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19251731>
Free article on PubMed Central: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2671989/>
- Thompson SW, Ruiz-Perez VL, Blair HJ, Barton S, Navarro V, Robson JL, Wright MJ, Goodship JA. Sequencing EVC and EVC2 identifies mutations in two-thirds of Ellis-van Creveld syndrome patients. *Hum Genet*. 2007 Jan;120(5):663-70. Epub 2006 Sep 21.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/17024374>
- Valencia M, Lapunzina P, Lim D, Zannolli R, Bartholdi D, Wollnik B, Al-Ajlouni O, Eid SS, Cox H, Buoni S, Hayek J, Martinez-Frias ML, Antonio PA, Temtamy S, Aglan M, Goodship JA, Ruiz-Perez VL. Widening the mutation spectrum of EVC and EVC2: ectopic expression of Weyer variants in NIH 3T3 fibroblasts disrupts Hedgehog signaling. *Hum Mutat*. 2009 Dec;30(12):1667-75. doi: 10.1002/humu.21117.
Citation on PubMed: <https://www.ncbi.nlm.nih.gov/pubmed/19810119>

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Reviewed: December 2012
Published: March 21, 2017

Lister Hill National Center for Biomedical Communications
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